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/ Ruth Montalvo Date: **June 30, 2004**

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Customer No.	026418		
Docket No.	GK-ZEI-3099 / 500343.20099		
Applicant(s):	Ralf WOLLESCHENSKY and Gunter MOEHLER		
Application No.:	09/895,517	Group:	2872
Filed:	June 28, 2001	Examiner:	Pritchett, J.
For:	METHOD FOR THE DETECTION OF DYES IN FLUORESCENCE MICROSCOPY		

Commissioner for Patents
Alexandria, VA 22313-1450

AMENDMENT

S I R:

In response to the Office Action dated December 31, 2004, please amend the application as follows.

Amendments to the specification:

Please insert the following new paragraph after page 8, line 21 and before page 8, line 22:

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Amendments to the claims:

1. (Currently Amended) A method for optical detection of ~~characteristic~~ quantities of different dyes in a specimen by detecting the wavelength-dependent behavior of an illuminated specimen in an image generating arrangement using spectra which contain overlapping dye spectra from different dyes which are simultaneously examined, ~~such as~~ the wavelength-dependent behavior including the emission behavior, absorption behavior, fluorescence, luminescence, phosphorescence, enzyme-active light emission, naturally occurring dye fluorescence from fluorescent proteins or enzyme-active fluorescence of the illuminated specimen, comprising:

determining at least one spectral centroid position for different dye spectra detected by a spectral detector wherein a characteristic dye spectra is detected for at least one image point of the specimen; and

applying a characteristic spectral weighting function to the characteristic dye spectra that is detected to separate overlapping dye components and to calculate the intensity of each dye component per desired image point.

2. (Currently Amended) The method according to claim 1, wherein the determination of the centroid position and of a maximum of the emission radiation of fluorochromes is carried out for distinguishing different dyes or for determining the local dye composition of an image point when a plurality of dyes are used simultaneously or for determining the local shift of the emission spectrum depending on the local environment to which the dye or dyes is or are attached or for measuring emission ratio dyes for determining ion concentrations.

3. (Currently Amended) The method according to claim 1, wherein the determination of the centroid position and of a maximum of the reflected or transmitted excitation radiation of fluorochromes is carried out for distinguishing different dyes or for determining the local dye composition of an image point when a plurality of dyes are used simultaneously or for determining the local shift in the absorption spectrum depending on the local environment to which the dye or dyes is or are attached or for measuring the absorption ratio for determining ion concentrations.

4. (Cancelled)

5. (Previously Presented) The method according to claim 1, further comprising splitting the fluorescent radiation.

6. (Previously Presented) The method according to claim 1, further comprising splitting the radiation reflected or transmitted by the specimen by a dispersive element for absorption measurement and detecting the split radiation in a spatially resolved manner in at least one direction.

7. (Previously Presented) The method according to claim 1, further comprising carrying out a spectral weighting between a plurality of detection channels,

summing of weighted channels of signals of the detection channels; and

summing of the detection channels.

8. (Previously Presented) The method according to claim 1, further comprising weighting the signals of the detection channels in that they are multiplied by a weighting curve,

generating a sum signal in that the sum of the channels taken into account is determined, and

generating a position signal in that the sum of weighted signals is divided by the sum signal.

9. (Original) The method according to claim 8, wherein the weighting curve is a straight line.

10. (Currently Amended) The method according to claim 1, further comprising:

converting signals of detection channels digitally;

reading out the signals of the detection channels ~~and;~~ ; and

weighting and summing the signals of the detection channels digitally in a computer.

11. (Previously Presented) The method according to claim 10, wherein the weighting and summing of the signals of the detection channels are carried out with analog data processing by

means of a resistance cascade.

12. (Currently Amended) The method according to claim 11, ~~further comprising adjusting the~~ wherein resistances of the resistance cascade means are adjustable.

13. (Previously Presented) The method according to claim 8, further comprising adjusting the weighting curve.

14. (Currently Amended) The method according to claim 1, further comprising influencing ~~the~~ signals of detector channels by a nonlinear distortion of the input signals.

15. (Previously Presented) The method according to claim 1, further comprising adjusting the integration parameters.

16. (Previously Presented) The method according to claim 1, further comprising adjusting a characteristic or response curve of an amplifier.

17. (Currently Amended) The method according to claim 8, further ~~comprising~~ comprising:

determining in analog ~~a~~ the position signal, ~~and;~~

determining in analog the sum signal,

converting to digital the position signal and the sum signal ~~and;~~ , and

reading out digitally the converted position signal and the sum signal.

18. (Previously Presented) The method according to claim 7, wherein an upper and a lower signal corresponding to the sum of the signals of individual channels which are weighted by opposing weighting curves are read out, digitally converted and fed to the computer.

19. (Previously Presented) The method according to claim 8, wherein a position signal and the sum signal are used to generate an image.

20. (Original) The method according to claim 1, wherein a color-coded fluorescence image is generated.

21. (Original) The method according to claim 1, wherein a superposition is carried out with additional images.

22. (Previously Presented) The method according to claim 8, wherein a position signal and the sum signal are combined with a lookup table.

23. (Original) The method according to claim 22, wherein representation of different dyes and/or the spread of the generated image is carried out by means of the lookup table.

24. (Currently Amended) The method according to claim 1, wherein a comparison of a measured signal with a reference signal is carried out via comparators in detection channels and in case the reference signal is not reached or is exceeded a change ~~in a~~ in an operating mode of a detection channel is carried out.

25. (Previously Presented) The method according to claim 24, wherein a respective detection channel is switched off or not taken into account.

26. (Previously Presented) The method according to claim 1, wherein a relevant spectral region is narrowed in this way.

27. (Previously Presented) The method according to claim 1, wherein signals of detection channels are generated by at least one integrator circuit.

28. (Previously Presented) The method according to claim 1, wherein signals of detection channels are generated by photon counting and subsequent digital-to-analog conversion.

29. (Previously Presented) The method according to claim 1, wherein a photon counting is carried out in time correlation.

30. (Currently Amended) The method according to claim 1, wherein the method is used for detection of single-photon ~~and/or~~ or multiphoton fluorescence ~~and/or~~ , or fluorescence excited

by entangled photons.

31. (Currently Amended) The method according to claim 1, wherein the method is used with parallel illumination and detection, in ingredient screening, wherein the specimen is a microtiter plate.

32. (Currently Amended) The method according to claim 1, wherein the method is used in a microscope.

33. (Currently Amended) The method according to claim 1, wherein the method is used for detection in a nearfield scanning microscope.

34. (Currently Amended) The method according to claim 1, wherein the method is used for detection of a single-photon ~~and/or~~ or multiphoton dye fluorescence in a fluorescence-correlated spectroscope.

35. (Currently Amended) The method according to claim 1, wherein the method uses ~~using~~ confocal detection.

36. (Currently Amended) The method according to claim 1, wherein the method uses ~~using~~ a scanning arrangement.

37. (Currently Amended) The method according to claim 1, wherein the method uses ~~using~~ an X-Y scanner in illumination means.

38. (Currently Amended) The method according to claim 1, wherein the method uses ~~using~~ an X-Y scan table.

39. (Currently Amended) The method according to claim 1, wherein the method uses ~~using~~ nonconfocal detection.

40. (Currently Amended) The method according to claim 1, wherein the method uses ~~using~~

a scanning arrangement.

41. (Currently Amended) The method according to claim 1, wherein the method uses ~~using~~ descanned detection.

42. (Currently Amended) The method according to claim 1, wherein the method uses ~~using~~ brightfield imaging.

43. (Currently Amended) The method according to claim 1, wherein the method uses ~~using~~ point imaging.

44. (Currently Amended) The method according to claim 1, wherein the method uses ~~using~~ non-descanned detection.

45. (Currently Amended) The method according to claim 1, wherein the method uses ~~using~~ brightfield imaging.

46. (Currently Amended) The method according to claim 1, wherein the method uses ~~using~~ non-scanning, confocal or nonconfocal detection and point imaging or brightfield imaging.

47. (Currently Amended) The method according to claim 1, wherein the method uses ~~using~~ an X-Y scan table.

48. (Currently Amended) An arrangement for optical detection of characteristic quantities of the wavelength-dependent behavior of an illuminated specimen using spectra which contain overlapping dye spectra from different dyes which are simultaneously examined, ~~particularly~~ the wavelength-dependent behavior including the emission behavior, absorption behavior, fluorescence, luminescence, phosphorescence, enzyme-active light emission, naturally occurring dye fluorescence from fluorescent proteins or enzyme-active fluorescence of an illuminated specimen, comprising:

an illumination source that provides an illumination for a specimen;

a spectral detector that receives detection radiation coming from the illuminated

specimen;

a computer ~~means~~ for determining at least one spectral centroid position for different dye spectra detected by the spectral detector wherein a characteristic dye spectra is detected for at least one image point of the specimen and the computer applies a characteristic spectral weighting function to the characteristic dye spectra that is detected to separate overlapping dye components and to calculate the intensity of each dye component per desired image point.

49. (Cancelled).

50. (Original) The arrangement according to claim 48, wherein a splitting of the fluorescent radiation is carried out.

51. (Original) The arrangement according to claim 48, wherein the radiation reflected or transmitted by the specimen is split by a dispersive element for absorption measurement and is detected in a spatially resolved manner in at least one direction.

52. (Currently Amended) The arrangement according to claim 48, wherein a spectral weighting is carried out between a plurality of detection channels, and summing of weighted channels of the signals of the detection channels is carried out and summing of detection channels is carried out.

53. (Previously Presented) The arrangement according to claim 52, wherein signals of detection channels are weighted in that they are multiplied by a weighting curve, a sum signal is generated in that the sum of the channels taken into account is determined, and a position signal is generated in that the sum of weighted signals is divided by the sum signal.

54. (Original) The arrangement according to claim 53, wherein the weighting curve is a straight line.

55. (Currently Amended) The arrangement according to claim 52, wherein signals of detection channels are converted and digitally read out and weighting and summing are carried out digitally ~~in a~~ by the computer.

56. (Original) The arrangement according to claim 52, wherein the weighting and summing are carried out with analog data processing by means of a resistance cascade.

57. (Previously Presented) The arrangement according to claim 56, wherein resistances are adjustable.

58. (Original) The arrangement according to claim 56, wherein the weighting curve is adjustable.

59. (Currently Amended) The arrangement according to claim 53, wherein ~~a~~ the position signal and the sum signal are determined in analog, converted, and read out digitally.

60. (Previously Presented) The arrangement according to claim 52, wherein an upper and a lower signal corresponding to the sum of the signals of individual channels which are weighted by opposing weighting curves are read out, digitally converted and fed to the computer.

61. (Currently Amended) The arrangement according to claim 53, wherein ~~a~~ the position signal and the sum signal are used to generate an image.

62. (Original) The arrangement according to claim 48, wherein a color-coded fluorescence image is generated.

63. (Original) The arrangement according to claim 48, wherein a superposition is carried out with additional images.

64. (Currently Amended) The arrangement according to claim 53, wherein ~~a~~ the position signal and the sum signal are combined with a lookup table.

65. (Original) The arrangement according to claim 64, wherein representation of different dyes and/or the spread of the generated image is carried out by the lookup table.

66. (Currently Amended) The arrangement according to claim 48, wherein a comparison of a measured signal with a reference signal is carried out via comparators in detection channels and in case the reference signal is not reached or is exceeded a change ~~in a~~ in an operating mode of a detection channel is carried out.

67. (Previously Presented) The arrangement according to claim 48, wherein a respective detection channel is switched off and/or not taken into account.

68. (Previously Presented) The arrangement according to claim 48, wherein a relevant spectral region is narrowed in this way.

69. (Original) The arrangement according to claim 48, wherein signals of detection channels are generated by at least one integrator circuit.

70. (Original) The arrangement according to claim 48, wherein signals of detection channels are generated by photon counting and subsequent digital-to-analog conversion.

71. (Previously Presented) The arrangement according to claim 70, wherein a photon counting is carried out in time correlation.

72. (Currently Amended) The arrangement according to claim 48, wherein the arrangement is used for detection of single-photon and/or multiphoton fluorescence and/or fluorescence excited by entangled photons.

73. (Currently Amended) The arrangement according to claim 48, wherein the arrangement is used with parallel illumination and detection, in ingredient screening, wherein the specimen is a microtiter plate.

74. (Currently Amended) The arrangement according to claim 48, wherein the arrangement is incorporated in a microscope.

75. (Currently Amended) The arrangement according to claim 74, wherein the arrangement

is used for detection in a nearfield scanning microscope.

76. (Currently Amended) The arrangement according to claim 48, wherein the arrangement is used for detection of a single-photon and/or multiphoton dye fluorescence in a fluorescence-correlated spectroscope.

77. (Currently Amended) The arrangement according to claim 48, wherein the arrangement incorporates ~~incorporating~~ confocal detection.

78. (Currently Amended) The arrangement according to claim 48, further comprising ~~including~~ a scanning arrangement coupled to the illumination source.

79. (Currently Amended) The arrangement according to claim 48, wherein the arrangement includes ~~including~~ an X-Y scanner ~~in~~ coupled to the illumination source.

80. (Currently Amended) The arrangement according to claim 48, further comprising ~~including~~ an X-Y scan table coupled to the illumination source.

81. (Currently Amended) The arrangement according to claim 48, wherein the arrangement incorporates ~~incorporating~~ nonconfocal detection.

82. (Currently Amended) The arrangement according to claim 48, wherein the arrangement is used with descanned detection.

83. (Currently Amended) The arrangement according to claim 48, wherein the arrangement is used with brightfield imaging.

84. (Currently Amended) The arrangement according to claim 48, wherein the arrangement is used with point imaging.

85. (Currently Amended) The arrangement according to claim 48, wherein the arrangement is used with non-descanned detection.

86. (Currently Amended) The arrangement according to claim 48, wherein the arrangement is used with non-scanning, confocal or nonconfocal detection and point imaging or brightfield imaging.

87 – 90. (Cancelled)

REMARKS

This application is related to U.S. application ser. no. 10/419,077, which is a continuation application of the present application.

In the continuation application, the Examiner has allowed all of the pending claims over the cited prior art. In the interest of advancing prosecution of the present application, Applicant has amended the pending claims so that they now track the allowed claims of the continuation application.

In the present Office Action, the Examiner rejected claims 1-47 and 87-89 under 35 U.S.C. Section 112, second paragraph, as being indefinite for using the word "such as". Applicant has amended the claims to remove such language.

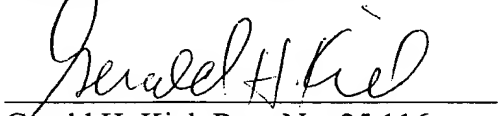
The Examiner rejected claims 48-86 and 90 under 35 U.S.C. Section 112, second paragraph, as being indefinite for failing to clearly define the wavelength dependent behavior. Applicant has amended claim 48 to delete the word "particularly" to make the claim more definite.

The Examiner rejected all pending claims under 35 U.S.C. Section 102(b) or Section 1032(a) under one or more of Jeffers, Yang, Okubo, Lee, Hochman, Kash, Simon, Yagi and Tuuanen. In view of the amendments that track the allowed claims of the continuation application, Applicant submits that these rejections are now moot.

Applicant is also submitting a color version of Figures. 13C and 13D under 37 C.F.R. Section 1.74 and MPEP Section 608.01(f) and respectfully requests the Examiner to enter the color figure version. A petition for admission of the color drawings is concurrently being submitted herewith.

Based upon the above amendments and remarks, Applicant respectfully requests reconsideration of this application and its early allowance. Should the Examiner feel that a telephone conference with Applicant's attorney would expedite prosecution of this application, the Examiner is urged to contact him at the number indicated below.

Respectfully submitted,



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